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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/593,629	06/13/2000	Don E. Carleton	01520.00372	7505

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EXAMINER
LE,QIAN J

ART UNIT	PAPER NUMBER
632	9

DATE MAILED: 04/24/2002

Please find below and or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/593,629	CAMERON ET AL
Examiner	**Art Unit**
Janice Li	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,13-17 and 19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,13-17 and 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ___
4)☐ Interview Summary (PTO-413) Paper No(s) ___
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other *detailed action*

DETAILED ACTION

The amendment filed on February 1, 2002 has been entered as Paper # 8. The examiner assigned to examine the application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to examiner Q. Janice Li, at Group Art Unit 1632.

Claims 1-7, 13, 14, 16, 19 and 24 have been amended. Claims 8-12 and 18 have been canceled. Claims 1-7, 13-17, and 19-24 are pending and under current examination.

Claim objections and rejections not reiterated in this Office action are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-5, 13-17, and 20-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "said engineered Sertoli tissue". There is insufficient antecedent basis for this limitation in the claim.

Claims 13-16 are drawn a method of making biochambers comprising co-culturing Sertoli cells and therapeutic cells such that an outer wall of Sertoli cells forms around the therapeutic cells. However, the method does not set forth any steps, thus, it

is unclear how co-culture would lead to the formation of said biochamber. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6. Likewise, claim 14 recites "the step of segregating the Sertoli cells away from the therapeutic cells, it is unclear how one could do that without setting forth positive steps.

Claim 14 recites the limitation "the step of segregating". There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites the limitation "the facilitator cells" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 17 recites "forming a biochamber", it is unclear with what material a biochamber is formed.

Claim 20 recites "a biochamber comprising an outer wall of protective cells and an inner wall of secreting cells". The description reads on a different structure comparing to the biochamber of claim 1, wherein here the wall of the biochamber comprises an outer layer of protective cells and an inner layer of secreting cells.

Claim 21 recites "a transplantation vessel comprising a housing made of one type of cell including an inner cavity and a center lumen. From the description, the structure of the housing could be interpreted as a smaller chamber (center lumen) surrounded by a larger chamber (inner cavity), it is another structure differing from the

structures described in claims 1 and 20. It is unclear whether applicants intend to claim three different tissue structures.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 13, 16, 19, 20-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The methodology for determining adequacy of Written Description to convey that applicant was in possession of the claimed invention includes determining whether the application describes an actual reduction to practice, determining whether the invention is complete as evidenced by drawings or determining whether the invention has been set forth in terms of distinguishing identifying characteristics as evidenced by other descriptions of the invention that are sufficiently detailed to show that applicant was in possession of the claimed invention (*Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, p 1 "Written Description" Requirement;* Federal Register/ Vol 66, No. 4, Friday, January 5, 2001; II Methodology for Determining Adequacy of Written Description (3.)).

Claims 1-7 and 19 are directed to a biochamber comprising a center lumen and outer walls formed of Sertoli cells. However, the specification does not provide and

adequate written description of the claimed invention. The term "chamber" means "a natural or artificial enclosed space or cavity", the term "lumen" means, "the cavity of a tubular organ" (Merriam-Webster's Collegiate Dictionary). With regard to claim recitation "a biochamber comprising a center lumen and outer walls formed of Sertoli cells", figures 1-3 illustrated diagrams of Sertoli cell behavior in the conventional and microgravity culture and when co-cultured with pancreatic islet cells, a center lumen surrounded by an outer wall of Sertoli cells was shown in these figures. However, figures 4 and 5 are photographs of a Sertoli-islet tissue construct by the conventional co-culture, although islet cells are in the center of the cell aggregates, there is no lumen in the construct. Likewise, figures 6 and 7 are photographs of microgravity culture showing Sertoli-neuron-aggregates without a center lumen. Apparently, the histological sections and microscopic photographs in the specification disclose cellular aggregates showing islet cells or neuronal cells surrounded by Sertoli cells, rather than "a biochamber comprising a center lumen".

Claim 20 recites "a biochamber comprising an outer wall of protective cells and an inner wall of secreting cells". From such description, a different structure is claimed comparing to the structure of claim 1, wherein here the wall of the biochamber comprises an outer layer of protective cells and an inner layer of secreting cells forming a chamber. Claim 21 recites "a transplantation vessel comprising a housing made of one type of cell including an inner cavity and a center lumen. From the description, the structure of the housing could be interpreted as a smaller chamber (center lumen) surrounded by a larger chamber (inner cavity). Apparently another structure is claimed

which differing from the structure described in claims 1 and 20. However, the specification fails to disclose such tissue structures.

Evidently, there are discrepancies between the diagrams and histological photographs of tissue constructs and among disclosed and claimed structures in the specification. A diagram is a drawing that shows arrangement and relations that explains rather than represents; whereas a photograph is an image of the subject. In view of such, the specification fails to provide an adequate written description of the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 16 recites "adding a compound for inducing epithelization and polarization". However, the specification fails to teach what are the compounds. Claims 20-24 recite a biochamber comprising an outer wall of protective cells and an inner wall of secreting cells. With respect to claim breadth given the broadest reasonable interpretation, the term "protective cells" reads on a genus of cells which act to protect secreting cells. the term compounds embraces a genus of molecules differing in chemical structures and physical properties. However, the only protective cells disclosed in the specification is the Sertoli cells, and the compounds have not been discussed in the specification.

An adequate written description for a compound or protective cells requires more than a mere statement that it is part of the invention; what is required is a description of the chemical structure of the compound, the histological, anatomical, and physiological

properties of the cell itself. It is not sufficient to define the compound or cells solely by its principal biological property, i.e. "inducing epitheliazation and polarization", "protective cells of secreting cells", because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any compound and any cell with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all compounds and cells that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). With respect to the method claims, adequate description of the methods first requires an adequate description of the materials, i.e. specific chemical and physical properties of a chemical, sequences of a protein and nucleic acids, and in the instant case, the type of cells which provide the means for practicing the invention. The court has made it very clear "CONCEPTION OF CHEMICAL COMPOUND REQUIRES THAT INVENTOR BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

The Revised Interim Guidelines state "THE CLAIMED INVENTION AS A WHOLE MAY NOT BE ADEQUATELY DESCRIBED IF THE CLAIMS REQUIRE AN ESSENTIAL OR CRITICAL ELEMENT WHICH IS NOT ADEQUATELY DESCRIBED IN THE SPECIFICATION AND WHICH IS NOT CONVENTIONAL IN THE ART" (Column 3, page 71434), "WHEN THERE IS SUBSTANTIAL VARIATION WITHIN THE GENUS, ONE

MUST DESCRIBE A SUFFICIENT VARIETY OF SPECIES TO REFLECT THE VARIATION WITHIN THE GENUS". "IN AN UNPREDICTABLE ART, ADEQUATE WRITTEN DESCRIPTION OF A GENUS WHICH EMBRACES WIDELY VARIANT SPECIES CANNOT BE ACHIEVED BY DISCLOSING ONLY ONE SPECIES WITHIN THE GENUS" (Column 2, page 71436).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad classes of *all* or representative species of compounds that induce polarization, and cells that protect secreting cells, and for the different biochamber structures. Therefore, only the described Sertoli cell and Sertoli-islet aggregates, Sertoli-neuron aggregates meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-7, 13-17, and 19-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way

as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided.

These claims are drawn to several biochambers with different tissue structures, compounds, and protective cells, however, as indicated *supra* in the written description section, the specification fails to provide an adequate description for the biochambers, compounds and cells encompassed by the claims. Therefore, one would not know how to use the invention without first carrying out undue experimentation to determine which chamber would be produced from co-culture of Sertoli cells and a type of therapeutic cells, and which compounds and cells have the recited characteristics. Claims 17, 21-24 are drawn to a method of transplanting a vessel of biochamber. however, as indicated *supra* in the written description section, the specification fails to provide an adequate description for what material forms the biochamber in claim 17, and all protective cells capable of forming such a chamber, one would not know how to use the invention without first carrying out undue experimentation to determine which chamber could be used in the claimed invention. Therefore, in view of the limited guidance, the lack of

predictability of the art, and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Claims 1-7, 17, and 19-24 are further drawn to therapeutic methods and composition. Claims 1-7, 19 recite "a biochamber", claim 21 recites "a transplant vessel, claims 17 recite "a method of transplanting cells". These claims clearly or implicitly state the intended use of the biochamber and methods. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. "WHEN A COMPOUND OR COMPOSITION CLAIM IS LIMITED BY A PARTICULAR USE, ENABLEMENT OF THAT CLAIM SHOULD BE EVALUATED BASED ON THAT USE". (MPEP 2164.01c) When analyzing the enabled scope of the claims, the intended use is to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. "a transplantation vessel" is defined as a composition for therapeutic use in cell transplantation to prevent, alleviate, treat, or cure a disease within the animal to which the substance is administered, therefore, will be evaluated by the standard. As such, the broadest reasonable interpretation of the claimed invention properly encompasses autologus and allogenic transplantation, and xenotransplantation in any subject including human, therefore, the claims will be evaluated by that standard.

In view of the state of the art and the levels of the skill in the art pertinent to Sertoli cell co-transplantation, significant progress has been demonstrated in the pertinent art. However, as *Willing et al* (Mol Med Today 1998 Nov;471-7) teach issues critical to the success in applying the method in humans remain to be addressed. For

example, it is unclear whether xenotransplantation could be tolerate in the present of Sertoli cells, whether Sertoli cells could survive a period long enough to achieve therapeutic effect in humans, whether the technique could be used for all types of diseases (see particular page 476, the outstanding questions). In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the references.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 13, 14, and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by *Korbutt et al* (Diabetologia 2000 Apr;43:474-80).

Claims 13 and 14 are drawn to a method of making biochambers comprising the step of co-culturing Sertoli cells and therapeutic cells such that an outer wall of Sertoli cells forms around the therapeutic cells, and including the step of segregating the Sertoli cells away from the therapeutic cells. Claim 19 is drawn to the biochamber produced.

Korbutt et al teach a method of co-culturing the Sertoli cells with islet cell preparation for three days before transplantation to allow Sertoli cells to aggregate (see last paragraph of the left column in page 475). *Korbutt et al* go on to teach that the transplants are in the form that the islet cells are surrounded by Sertoli cells (see particularly figs 2c-d). Therefore, *Korbutt et al* anticipate these claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
April 16, 2002

JAMES KETTER
PRIMARY EXAMINER